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BY: JMeier

Date: 3/15/02

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of:
CLAESSENS, Johannes A.J.
FUCHS, Walter

Serial Number: To be assigned Group Art Unit: To be assigned

Filed: concurrently herewith Examiner: To be assigned

For: RECOMBINANT INFECTIOUS LARYNGOTRACHEITIS VIRUS VACCINE

Corresponding to: EP01200975.9, Filed 15 March, 2001

PRELIMINARY AMENDMENT

Assistant Commissioner of Patents
Washington, D.C. 20231

March 15, 2002

Sir:

Applicants are hereby including this preliminary amendment to the enclosed US filing of European patent application number 01200975.9 filed on March 15, 2001. Filed with this preliminary amendment is a copy of the original specification from the European patent application, a certified copy of the priority document filed in the European patent office, declarations and power of attorney from all the inventors, assignments from all the inventors, IDS, PTO form 1449, cited references, and a sequence listing in computer readable format (CRF) and paper copy. Please charge all required fees to Deposit Account No. 02-2334.

I. In the Claims (Clean Sheet):

11. A vaccine for the protection of poultry against disease caused by an avian pathogen comprising an attenuated infectious laryngotracheitis virus (ILTV) mutant and a pharmaceutically acceptable carrier or diluent, characterized in that the ILTV mutant is not able to express a native UL0 protein in an infected host cell as a result of a mutation in the UL0 gene.

12. A vaccine according to Claim 11, characterized in that the mutation in the UL0 gene is a deletion.

13. A vaccine according to Claim 11, characterized in that the mutation in the UL0 gene is an insertion of a heterologous nucleic acid sequence.

14. A vaccine according to Claim 12, characterized in that the mutant comprises a heterologous nucleic acid sequence in place of the deletion

15. A vaccine according to Claim 13, characterized in that the heterologous nucleic acid sequence is under the control of an expression control sequence.

16. A vaccine according to Claim 14, characterized in that the heterologous nucleic acid sequence is under the control of an expression control sequence.

17. A vaccine according to Claim 15, characterized in that the heterologous nucleic acid sequence encodes an antigen of an avian pathogen.

18. A vaccine according to Claim 16, characterized in that the heterologous nucleic acid sequence encodes an antigen of an avian pathogen.

19. A vaccine according to Claim 17, characterized in that the avian pathogen is avian influenza virus, Marek's disease virus, Newcastle disease virus, infectious bronchitis virus, turkey rhinotracheitis virus, E.coli, Ornithobacterium rhinotracheale or Mycoplasma.

20. A vaccine according to Claim 18, characterized in that the avian pathogen is avian influenza virus, Marek's disease virus, Newcastle disease virus, infectious bronchitis virus, turkey rhinotracheitis virus, E.coli, Ornithobacterium rhinotracheale or Mycoplasma.

21. A vaccine according to Claim 15, characterized in that the heterologous nucleic acid sequence encodes an immunomodulator.

22. A vaccine according to Claim 16, characterized in that the heterologous nucleic acid sequence encodes an immunomodulator.

23. A cell culture infected with an ILTV mutant as defined in any one of Claims 11-22.

24. A process for the preparation of a vaccine for the protection of poultry against disease caused by an avian pathogen, characterized in that it comprises the step of mixing an ILTV mutant as defined in any one of Claims 11-22 with a pharmaceutically acceptable carrier or diluent.

II. IN THE CLAIMS (MARKED VERSION):

Please cancel claims 1-10 without prejudice or disclaimer. Such cancellation is to place the claims in a condition for US examination and was not done for any reason related to patentability under 35 USC §§101, 102, 103, and/or 112. No estoppel should result from this preliminary amendment.

Please insert the following claims.

- -11. A vaccine for the protection of poultry against disease caused by an avian pathogen comprising an attenuated infectious laryngotracheitis virus (ILTV) mutant and a pharmaceutically acceptable carrier or diluent, characterized in that the ILTV mutant is not able to express a native UL0 protein in an infected host cell as a result of a mutation in the UL0 gene.

12. A vaccine according to Claim 11, characterized in that the mutation in the UL0 gene is a deletion.

13. A vaccine according to Claim 11, characterized in that the mutation in the UL0 gene is an insertion of a heterologous nucleic acid sequence.

14. A vaccine according to Claim 12, characterized in that the mutant comprises a heterologous nucleic acid sequence in place of the deletion

15. A vaccine according to Claim 13, characterized in that the heterologous nucleic acid sequence is under the control of an expression control sequence.

16. A vaccine according to Claim 14, characterized in that the heterologous nucleic acid sequence is under the control of an expression control sequence.

17. A vaccine according to Claim 15, characterized in that the heterologous nucleic acid sequence encodes an antigen of an avian pathogen.

18. A vaccine according to Claim 16, characterized in that the heterologous nucleic acid sequence encodes an antigen of an avian pathogen.

19. A vaccine according to Claim 17, characterized in that the avian pathogen is avian influenza virus, Marek's disease virus, Newcastle disease virus, infectious bronchitis virus, turkey rhinotracheitis virus, E.coli, Ornithobacterium rhinotracheale or Mycoplasma.

20. A vaccine according to Claim 18, characterized in that the avian pathogen is avian influenza virus, Marek's disease virus, Newcastle disease virus, infectious bronchitis virus, turkey rhinotracheitis virus, E.coli, Ornithobacterium rhinotracheale or Mycoplasma.

21. A vaccine according to Claim 15, characterized in that the heterologous nucleic acid sequence encodes an immunomodulator.

22. A vaccine according to Claim 16, characterized in that the heterologous nucleic acid sequence encodes an immunomodulator.

23. A cell culture infected with an ILTV mutant as defined in any one of Claims 11-22.

24. A process for the preparation of a vaccine for the protection of poultry against disease caused by an avian pathogen, characterized in that it comprises the step of mixing an ILTV mutant as defined in any one of Claims 11-22 with a pharmaceutically acceptable carrier or diluent. - -

III. In the Specification (Clean Sheet):

(Page 1, line 1)

Field of the Invention

The present invention is concerned with a vaccine for the protection of poultry caused by an avian pathogen comprising an attenuated infectious laryngotracheitis virus (ILTV) mutant and a pharmaceutically acceptable carrier or diluent, a cell culture infected with an attenuated ILTV mutant as well as a process for the preparation of such a vaccine.

(Page 1, line 7)

Background of the Invention

Infectious laryngotracheitis (ILT) is a respiratory disease that mainly affects chickens, but pheasants and peacocks can also be infected. In the acute phase of the disease, from 2 to 8 days post-infection, signs of respiratory distress accompanied by gasping and expectoration of bloody exudate is are observed. In addition, the mucous membranes of the trachea become swollen and hemorrhagic. This epizootic form of the disease spreads rapidly and can affect up to 100% of an infected flock. Mortality can range from 10 to 80% of the flock. Milder forms of the disease are characterized by watery eyes, conjunctivitis, persistent nasal discharge and a reduction in egg production. Also weight loss, drop in egg production and increased sensitivity to secondary infection are major causes of economic losses.
In the absence of the acute signs of the disease laboratory confirmation must be obtained. Virus can be readily isolated from tracheal or lung tissue and the demonstration of intranuclear inclusion bodies in tracheal or conjunctival tissue

is diagnostic in infectious laryngotracheitis virus. In addition, rapid identification can be made with the use of fluorescent antibodies.

(Page 3, line 19)

Summary of the Invention

It is an object of the present invention to provide a vaccine that comprises an ILTV vaccine strain that is attenuated in a controlled way by means of genetic engineering techniques that prevent a reversion to virulence of the attenuated vaccine strain, and that is able to induce a protective immune response in a host animal infected with the vaccine strain.

(Page 3, line 32)

Detailed Description

The inventors have found that, in contrast to the UL[-1] gene, the ILTV-specific UL0 gene is not only non-essential for ILTV infection or replication in cells but that, in addition, the inactivation of the expression of the native UL0 protein by means of controlled genetic engineering of the UL0 gene results in an ILTV mutant that is attenuated when compared to wild-type parent ILTV. Furthermore, it is found that this attenuated ILTV mutant is able to induce a protective immune response that reduces mortality and clinical signs in vaccinated animals upon challenge with virulent ILTV. In addition, the vaccine according to the present invention displays a further advantage in that it can be administered safely to chickens via spray mass-vaccination.

(Page 12, line 1)

Brief Description of the Figures

Figure 1

Genomic map of ILTV genome and construction of the transfer plasmids. The relevant restriction sites for generation of the transfer plasmids, the heterologous sequences, promoters and poly-A signals are indicated. ILTV recombinants (names in bold italics) could be isolated after cotransfection of cells with transfer plasmids and virion-DNA.

IV. In the Specification (Marked Version):

Please insert "Field of the Invention", as a new line, at line 1, page 1.

Please insert "Background of the Invention", as a new line, at line 6 of page 1.

Please insert "Summary of the Invention", as a new line, at line 19 of page 3.

Please insert "Detailed Description", as a new line, at line 32 of page 3.

Please delete "Legends to the figures" at line 1 of page 12.

Please insert "Brief Description of the Figures", as a new line, at line 1 of page 12.

V. Remarks

Applicants' US filing is a duplicate copy of the originally filed European patent application. Applicants have preliminarily amended the claims to the originally filed European patent application to place the claims in proper condition for U.S examination. The amendments to the claims and the specification were not made for reasons of patentability under 35 U.S.C. §§ 101, 102, 103 and/or 112. No estoppel should result from the amendments.

Respectfully submitted,

William P Ramey III
Patent Counsel
Registration No. 44,295

Attorney Docket NO. 2001.001 US

Intervet Inc Patent Department
Akzo Nobel
405 State Street
P.O. Box 318
Millsboro, DE 19966
Tel: (302) 933-4034
Fax: (302) 933-4013

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